UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,405	05/04/2005	Dale L Boger	TSRI 880.1	7486

26621 7590 02/11/2008

THE SCRIPPS RESEARCH INSTITUTE
OFFICE OF PATENT COUNSEL, TPC-8
10550 NORTH TORREY PINES ROAD
LA JOLLA, CA 92037

EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
02/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,405	BOGER ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims 6-7 are drawn to 'a method of inhibiting glycinamide ribonucleotide transformylase or aminoimidazole carboxamide ribonucleotide transformylase' and the specification provides that this biological activity is related to chemotherapeutic agents for

cancer treatment. First, the instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through to the corresponding therapeutic method of any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

The testing assays provided in the specification are to test the ability of the compounds to inhibit GAR Tfase activity using in for example, CCRF-CEM cell lines *in vitro*, however, there is insufficient guidance in the disclosure regarding the test assays and the corresponding therapeutic activity. Applicant has not provided how this correlates with the efficacy in all types of hosts and subjects encompassed by the instant method and their use in the various purposes wherein the inhibition activity is useful. As can be seen from the above, without limitation these purposes are intended for therapeutic methods and applicant has not provided competent evidence sufficient to enable the claimed method.

The instant claims are read on many therapeutic methods, for example, a method of treating cancer, etc. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). A 'disorder characterized by abnormal cell proliferation' is anything that is caused by abnormal tissue growth. That can be growth by

cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers or abnormal cell proliferative disorders generally.

Further, there is no disclosure regarding how the patient in need of the treatment requiring the specific GAR Tfase inhibiting activity is identified and further, how all types of the diseases having diverse mechanisms are treated. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area, and the data provided of the single compound is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment. Next, applicant's attention is drawn to the "Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001"

wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly intended medicinal use of chemotherapeutic drug design solely based on the kinase inhibitory activity disclosed for the compounds.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

2. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound represented by the structure depicted in claim 1, does not reasonably provide enablement for a **complex** comprising glycinamide ribonucleotide transformylase and the compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant claim is drawn to 'a complex comprising glycinamide ribonucleotide transformylase and the compound' and there is insufficient enablement in the specification regarding the types of "complexes" intended by the claims. The specification in Figure 19, indicates a few examples to form the corresponding complexes of the compound, however, there is no description of all types of complexes of the instant compounds or a method of preparation of the same. There is neither a procedure describing how such "complexes" are prepared nor examples that illustrate the same. Further, the instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to a characteristic or functionality of the compound and thereby reach through to all types of compounds, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention. Applicant has neither described nor provided working examples for the 'complex' of all of the invention compounds with glycinamide ribonucleotide transformylase intended by the instant claim language. These types of complexes do not depend on the novelty of the claimed compounds for patentability, but instead require separate inventive effort and are patentable over the claimed compounds. The disclosure therefore cannot rely on the state of the art in providing the necessary description of the types of

'complexes' intended by the instant claims. None of the types of 'complexes' recited in the claims were prepared by applicants or specifically suggested in the disclosure.

The specification fails to enable the preparation of the entire scope of the claimed compounds, specifically the complexes. The preparation and biological activity disclosed in the specification is with respect to the compounds as recited in claims 1-5. There is no disclosure of the types of complexes intended by the claim; a procedure to prepare the same; or examples illustrating the types of complexes intended by the instant claims. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); *Ex parte Moersch*, 104 USPQ 122 (POBA 1954).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. The structures depicted in claims 4 and 5 are not consistent with the structures disclosed in the specification at pages 8-9 respectively. The square brackets are not positioned correctly and therefore, the claims are confusing.
2. Claims 6-7 are drawn to 'a process for inhibiting', however, do not recite where the 'inhibition' is intended to take place. The claims do not recite any host or subject.
3. Claim 8 is drawn to a 'complex', however, it is not clear what type of complex is intended. The specification does not provide any explanation or an example of a complex.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

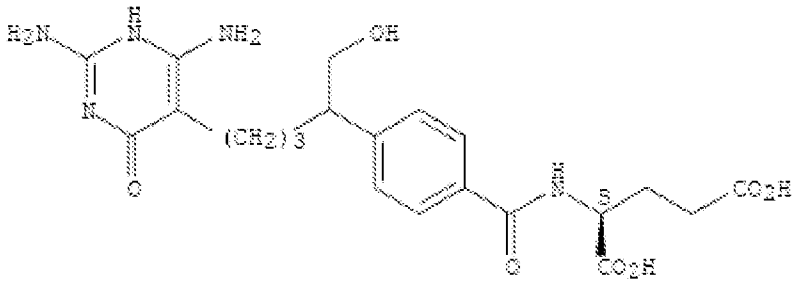
1. Claims 1-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marsilje et al. (Bioorganic & Medicinal Chemistry, August 2002). The instant claims read on reference disclosed compounds, see the compounds disclosed in the reference.

Note: Applicant cannot rely on the benefit of priority based on Provisional Application 60/370,591 (filed April 5, 2002) to overcome the above rejections under 35 U.S.C. 102(a), as the Provisional application does not fully support the instantly claimed invention. See, for example, the application does not disclose a genus as claimed in claim 1 (of the structural formula depicted

in claim 1). Therefore, the effective filing date for the instant application is the filing date of the International application, i.e., April 7, 2003.

2. Claims 1 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al., U.S. Patent No. 5,013,738. The instant claims read on reference disclosed compounds, see the compound of Example 3 B (depicted below for convenience):

B.
N-{4-[1-Hydroxy-5-2,6-diamino-4-hydroxypyrimidin-5-yl]pent-2-yl]benzoyl}-L-glutamic acid



The compounds are taught to be useful as antineoplastic agents. Claims 6-7 are drawn to 'a method of inhibiting' and the specification provides that due to the biological activity, the compounds are useful as medicinal agents for treatment of cancer. Therefore, claims 6-7 are drawn to a method wherein the compound is administered to the same patient population.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

February 10, 2008